

63. (New) The adenoviral capsid of claim 62, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

64. (New) An adenoviral vector comprising the adenoviral capsid of claim 62 and an adenoviral genome.

REMARKS

The Present Invention

The present invention is directed to a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence. The non-native amino acid sequence encodes a ligand that binds to a substrate present on the surface of a cell. Additionally, the non-native amino acid sequence constitutes the C-terminus of the chimeric protein, the N-terminus of the chimeric protein, or is located internally within the chimeric protein. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence also is provided, as well as a composition comprising the adenoviral capsid, an adenoviral vector comprising the adenoviral capsid, and a method of infecting a cell.

The Pending Claims

Claims 1, 4-7, 9-13, 15, 17-29, 31-35, 37-39, 41-42, and 46-64 are currently pending and are directed to the chimeric pIX protein (claims 1, 4-7, 9-17, 41-42 and 46-47, 49-51, and 56-60), the nucleic acid encoding the chimeric pIX protein (claims 18, 48, 52, and 61), the adenoviral capsid (claims 19-28, 53, 54, 62, and 63), the composition comprising the adenoviral capsid (claim 29), the adenoviral vector comprising the adenoviral capsid (claims 31-35, 37, 38, 55, and 64), and the method of infecting a cell (claim 39).

The Amendments to the Claims

Claims 1, 9, 10, 19, and 42 have been amended to point out more particularly and claim more distinctly the present invention. Claims 1 and 19 have been amended to incorporate the features of claim 8, which has been cancelled. Claims 9 and 10 have been rewritten in independent form. Claim 42 has been amended to incorporate the features of claims 43 and 44, which have been cancelled. Claims 49-64 are new and have been added in view of the amendments to claims 1 and 19. Claims 49-64 are supported by the specification at, for example, pages 3-4, paragraphs 0008-0012, and page 8, paragraph 0019. Claim 59

incorporates the features of claim 16, which has been cancelled. Claims 8, 14, 16, 30, 36, 40, and 43-45 have been cancelled. No new matter has been added by way of these amendments. Separate documents setting forth the precise amendments to the claims, as well as the text of all of the pending claims as amended, are enclosed.

The Office Action

The Office has rejected claims 1, 5, 18-19, 29, 30-32, and 34-40 as being allegedly anticipated by the Romanczuk reference (WO 99/36545) under 35 U.S.C. § 102(a). The Office has objected to claims 4, 6-17, 20-28, and 33 as being dependent upon a rejected base claim. Claims 41-48 have been allowed. Reconsideration of the rejection and objection is hereby requested.

Discussion of the Rejection

Claims 1, 5, 18-19, 29, 30-32, and 34-40 have been rejected by the Office as being allegedly anticipated by the Romanczuk reference (WO 99/36545) under 35 U.S.C. § 102(a).

The Office contends that the Romanczuk reference discloses several elements of the present invention, including a chimeric pIX protein having at least one pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell, nucleic acids encoding the chimeric pIX protein, an adenoviral capsid containing the chimeric pIX protein, compositions comprising the capsid, adenoviral vectors comprising the chimeric pIX protein, and methods of infecting a cell comprising contacting a cell with the adenoviral vector (Office Action dated September 7, 2002, page 2, last complete paragraph).

Claims 1 and 19 have been amended to recite that the non-native amino acid sequence of the chimeric pIX protein constitutes the C-terminus of the chimeric protein. The Romanczuk reference does not teach or suggest a chimeric pIX protein in which the non-native amino acid sequence constitutes the C-terminus of the protein. The Office has recognized this deficiency in the Romanczuk reference by indicating that claim 8 (the features of which have been incorporated into claims 1 and 19) would be allowable if written in independent form. Therefore, claims 1 and 19, as well as claims 5, 18, 29, 30-32, and 34-40 dependent thereon are not anticipated by the Romanczuk reference, and the rejection under Section 102(a) should be withdrawn.

The Office has objected to claims 4, 6-17, 20-28, and 33 as being dependent on a rejected base claim. Claims 9 and 10 have been re-written in independent format as suggested by the Office. The Romanczuk reference does not teach or suggest the subject

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Application No. 09/780,224

matter of claims 4, 6, 7, 9-17, 20-28, and 33, or new claims 49-64. Accordingly, Applicants request an indication of allowability of these claims.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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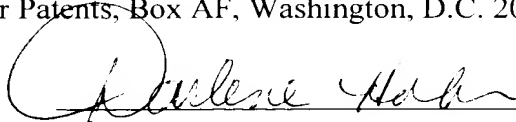
Date: November 18, 2002

CERTIFICATE OF MAILING

I hereby certify that this RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Box AF, Washington, D.C. 20231.

Date:

11/18/02



**RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1636**

PATENT
Attorney Docket No. 208859

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Roelvink et al.

Art Unit: 1636

Application No. 09,780,224

Examiner: Guzo, David

Filed: February 9, 2001

For: ADENOVIRAL CAPSID
CONTAINING CHIMERIC PROTEIN
IX

**AMENDMENTS TO CLAIMS
MADE IN RESPONSE TO OFFICE ACTION DATED AUGUST 17, 2002**

Amendments to existing claims:

1. (Twice Amended) A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.

[8. (Cancelled) The chimeric pIX protein of claim 1, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.]

9. (Amended) [The chimeric pIX protein of claim 1,] A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell, wherein the non-native amino acid sequence constitutes the N-terminus of the chimeric protein.

10. (Amended) [The chimeric pIX protein of claim 1,] A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a

ligand that binds to a substrate present on the surface of a cell, wherein the non-native amino acid sequence is located internally within the chimeric protein.

[14. (Cancelled) The chimeric pIX protein of claim 13, wherein the first and the second adenoviral pIX domains do not share any common peptide sequences.]

[16. (Cancelled) The chimeric pIX protein of claim 15, wherein the spacer peptide domain comprises the ligand domain.]

19. (Twice Amended) An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.

[30. (Cancelled) The composition of matter of claim 29, further comprising a liposome.]

[36. (Cancelled) The adenoviral vector of claim 35, having a ligand that binds to a substrate present on the surface of a cell and wherein the non-adenoviral promoter is active within the cell.]

[40. (Cancelled) The method of claim 39, wherein the adenoviral genome comprises a non-native nucleic acid encoding a protein, and wherein the nucleic acid is expressed within the cell to produce the protein.]

42. (Amended) The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

[43. (Cancelled) The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.]

[44. (Cancelled) The chimeric pIX protein of claim 41, comprising a first adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence

truncated at the C-terminus and a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.]

[45. (Cancelled) The chimeric pIX protein of claim 44, wherein the first and the second adenoviral pIX domains do not share any common peptide sequences.]

49. (New) The chimeric pIX protein of claim 9, wherein the ligand is an RGD-containing or polylysine-containing sequence.

50. (New) The chimeric pIX protein of claim 9, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

51. (New) The chimeric pIX protein of claim 9, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

52. (New) A nucleic acid encoding the chimeric pIX protein of claim 9.

53. (New) An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence constitutes the N-terminus of the chimeric protein.

54. (New) The adenoviral capsid of claim 53, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

55. (New) An adenoviral vector comprising the adenoviral capsid of claim 53 and an adenoviral genome.

56. (New) The chimeric pIX protein of claim 10, wherein the ligand is an RGD-containing or polylysine-containing sequence.

57. (New) The chimeric pIX protein of claim 10, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a

second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

58. (New) The chimeric pIX protein of claim 57, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus, and a spacer peptide domain separates the first and the second adenoviral pIX domains.

59. (New) The chimeric pIX protein of claim 58, wherein the spacer peptide domain comprises the ligand domain.

60. (New) The chimeric pIX protein of claim 10, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

61. (New) A nucleic acid encoding the chimeric pIX protein of claim 10.

62. (New) An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence is located internally within the chimeric protein.

63. (New) The adenoviral capsid of claim 62, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

64. (New) An adenoviral vector comprising the adenoviral capsid of claim 62 and an adenoviral genome.

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Art Unit: 1636

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For: ADENOVIRAL CAPSID
CONTAINING CHIMERIC PROTEIN
IX

**PENDING CLAIMS AFTER AMENDMENTS
MADE IN RESPONSE TO OFFICE ACTION DATED AUGUST 17, 2002**

1. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.

4. The chimeric pIX protein of claim 1, wherein the ligand recognizes a CD40 protein.

5. The chimeric pIX protein of claim 1, wherein the ligand is an RGD-containing or polylysine-containing sequence.

6. The chimeric pIX protein of claim 1, wherein the non-native amino acid is constrained by a peptide loop within the chimeric protein.

7. The chimeric pIX protein of claim 6, wherein the loop comprises a disulfide bond between non-adjacent amino acids of the protein.

9. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface

of a cell, wherein the non-native amino acid sequence constitutes the N-terminus of the chimeric protein.

10. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding a ligand that binds to a substrate present on the surface of a cell, wherein the non-native amino acid sequence is located internally within the chimeric protein.

11. The chimeric pIX protein of claim 1, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus.

12. The chimeric pIX protein of claim 1, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

13. The chimeric pIX protein of claim 1, comprising a first adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the C-terminus and a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

15. The chimeric pIX protein of claim 13, wherein a spacer peptide domain separates the first and the second adenoviral pIX domains.

17. The chimeric pIX protein of claim 1, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

18. A nucleic acid encoding the chimeric pIX protein of claim 1.

19. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric protein.

20. The adenoviral capsid of claim 19, which binds dendritic cells.

21. The adenoviral capsid of claim 19, comprising a mutant adenoviral fiber protein having an affinity for a native adenoviral cellular receptor of at least about an order of magnitude less than a wild-type adenoviral fiber protein.

22. The adenoviral capsid of claim 19, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

23. The adenoviral capsid of claim 19, comprising an adenoviral hexon protein having a mutation affecting at least one native HVR sequence.

24. The adenoviral capsid of claim 19, lacking a native glycosylation or phosphorylation site.

25. The adenoviral capsid of claim 19, which is conjugated to polyethylene glycol.

26. The adenoviral capsid of claim 19, which elicits less immunogenicity in a host animal than does a wild-type adenovirus.

27. The adenoviral capsid of claim 19, comprising a second non-adenoviral ligand conjugated to a fiber, a penton, a hexon, a protein IIIa or a protein VI.

28. The adenoviral capsid of claim 27, wherein the non-native amino acid is a ligand and wherein the second non-adenoviral ligand recognizes the same substrate as the non-native amino acid.

29. A composition of matter comprising the adenoviral capsid of claim 19 and a nucleic acid.

31. An adenoviral vector comprising the adenoviral capsid of claim 19 and an adenoviral genome.

32. The adenoviral vector of claim 31, which is replication incompetent.

33. The adenoviral vector of claim 31, which does not productively infect HEK-293 cells.

34. The adenoviral vector of claim 31, wherein the adenoviral genome comprises a non-native nucleic acid for transcription.

35. The adenoviral vector of claim 34, wherein the non-native nucleic acid for transcription is operably linked to a non-adenoviral promoter.

37. The adenoviral vector of claim 35, wherein the non-adenoviral promoter is a tissue-specific promoter.

38. The adenoviral vector of claim 35, wherein the non-adenoviral promoter is a regulable promoter.

39. A method of infecting a cell, comprising contacting a cell with an adenoviral vector of claim 31.

41. A chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence encoding an antigen, wherein the non-native amino acid sequence constitutes the C-terminus of the chimeric pIX protein or is located internally within the chimeric pIX protein.

42. The chimeric pIX protein of claim 41, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

46. The chimeric pIX protein of claim 44, wherein a spacer peptide domain separates the first and the second adenoviral pIX domains.

47. The chimeric pIX protein of claim 41, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

48. A nucleic acid encoding the chimeric pIX protein of claim 41.

49. The chimeric pIX protein of claim 9, wherein the ligand is an RGD-containing or polylysine-containing sequence.

50. The chimeric pIX protein of claim 9, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

51. The chimeric pIX protein of claim 9, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

52. A nucleic acid encoding the chimeric pIX protein of claim 9.

53. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence constitutes the N-terminus of the chimeric protein.

54. The adenoviral capsid of claim 53, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

55. An adenoviral vector comprising the adenoviral capsid of claim 53 and an adenoviral genome.

56. The chimeric pIX protein of claim 10, wherein the ligand is an RGD-containing or polylysine-containing sequence.

57. The chimeric pIX protein of claim 10, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence (a) truncated at the C-terminus, (b) truncated at the N-terminus, or (c) truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX peptide sequence truncated at the N-terminus.

58. The chimeric pIX protein of claim 57, wherein at least one adenoviral pIX domain consists essentially of an adenoviral pIX peptide sequence truncated at the C-terminus with a second adenoviral pIX domain consisting essentially of an adenoviral pIX

peptide sequence truncated at the N-terminus, and a spacer peptide domain separates the first and the second adenoviral pIX domains.

59. The chimeric pIX protein of claim 58, wherein the spacer peptide domain comprises the ligand domain.

60. The chimeric pIX protein of claim 10, having only one adenoviral pIX domain consisting essentially of a full-length adenoviral pIX peptide sequence.

61. A nucleic acid encoding the chimeric pIX protein of claim 10.

62. An adenoviral capsid containing a chimeric pIX protein having at least one adenoviral pIX domain and a non-native amino acid sequence, wherein the non-native amino acid sequence is located internally within the chimeric protein.

63. The adenoviral capsid of claim 62, comprising an adenoviral penton base protein having a mutation affecting at least one native RGD sequence.

64. An adenoviral vector comprising the adenoviral capsid of claim 62 and an adenoviral genome.